



I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: MS Missing Parts, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date shown below.

Dated: 6/10/04 Signature: *Ginny Blundell*
(Ginny Blundell)

Docket No.: HMSU-P17-006
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Ingham et al.

Application No.: 10/647654

Confirmation No.: 5276

Filed: August 25, 2003

Art Unit: 1646

For: VERTEBRATE EMBRYONIC PATTERN
INDUCING PROTEINS AND USES
RELATED THERETO

Examiner: C. M. Kaufman

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 CFR 1.97(b)(3)).

Copies of the references on the PTO/SB/08 are not provided because they were previously cited by or submitted to the Office in a prior application number 08/954128, filed October 20, 1997 and relied upon in this application for an earlier filing date under 35 U.S.C. 120.

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information

as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR 1.97(h), the filing of this Information Disclosure statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, under Order No. HMSU-P17-006.

Dated: June 10, 2004

Respectfully submitted,

By 

Melissa S. Rones, Ph.D.

Registration No.: 54,408
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant

Form PTO-1449

**INFORMATION DISCLOSURE
CITATION
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number (Optional)

HMV-006.12

Application Number

08/954,128

Applicant Ingham, Philip, et al.

Filing Date 20 October 1997

Group Art Unit

U.S. PATENT DOCUMENTS

EXAM. INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AA	5,223,408	6/29/93	Goeddel et al.	435	69.3	
AB	5,585,087	12/17/96	Lustig et al.	424	9.2	
AC						
AD						
AE						

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
AF	WO 90/02809	3/22/90	PCT	C12P	21/00		
AG	WO 92/15679	9/17/92	PCT	C12N	15/10		
AH							
AI							
AJ							

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

AK	Anderson, R. et al., "Maintenance of ZPA signaling in cultured mouse limb bud cells", <i>Devel.</i> <u>117</u> :142-1433 (1993).
AL	Angier, N. "Biologists find key genes that shape patterning of embryos", <i>New York Times</i> , Jan 11, 1994, C-1.
AM	Basler, K. and G. Struhl, "Compartment boundaries and the control of <i>Drosophila</i> limb pattern by <i>hedgehog</i> protein", <i>Nature</i> <u>368</u> : 208-214 (1994).
AN	Basler, K. et al., "Control of cell pattern in the neural Tube: Regulation of cell differentiation by <i>dorsalin-1</i> , a novel TGF β family member", <i>Cell</i> <u>73</u> :687-702 (1993).
AO	Bass, S. et al., "Hormone phage: An Enrichment Method for Variant Proteins with Altered Binding Properties", <i>PROTEINS: Structure, Function, and Genetics</i> <u>8</u> :309-314 (1990).
AP	Bejsovec, A. and E. Wieschaus, "Segment polarity gene interactions modulate epidermal patterning in <i>Drosophila</i> embryos", <i>Devel.</i> <u>119</u> :501-517 (1993).
AQ	Bienzi, M., "Homeotic genes and positional signalling in the <i>Drosophila</i> viscera", <i>TIG</i> <u>10</u> :22-26 (Jan. 1994).
AR	Bitgood, M. and McMahon, A., "Hedgehog and Bmp Genes are Coexpressed at Many Diverse Sites of Cell-Cell Interaction in the Mouse Embryo", <i>Dev. Biol.</i> <u>172</u> (1):126-138 (1995).
AS	Blair, S.S., "Hedgehog digs up an old friend", <i>Nature</i> <u>373</u> :656-657 (23 Feb.1995).
AT	Bone et al., <i>Endo. Meta.</i> <u>2</u> :160-184 (1995).
AU	Brand-Saberi, B. et al., "The ventralizing effect of the notochord on somite differentiation in chick embryos", <i>Anat. Embryol.</i> <u>188</u> : 239-245 (1993).
AV	Brookes, J., "We may not have a morphogen", <i>Nature</i> <u>350</u> :15 (1991).
AW	Bumcrot, D.A. and McMahon A. "Sonic Hedgehog: Making the gradient", <i>Chem. Biol.</i> <u>3</u> (1):13-16 (Jan 1996).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP \square 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Docket Number (Optional) HMV-006.12	Application Number 08/954,128
		Applicant Ingham, Philip, et al.	
		Filing Date 20 October 1997	Group Art Unit
OTHER DOCUMENTS <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>			
AX	Bumcrot, D.A. and McMahon, A., "Somite differentiation. Sonic signals somites", <i>Curr. Biol.</i> <u>5</u> (6):612-614 (June 1995).		
AY	Bumcrot, D.A. et al., "Proteolytic processing yields two secreted forms of sonic hedgehog", <i>Mol. Cell. Biol.</i> <u>15</u> (4):2294-2303 (4/95).		
AZ	Charité, J. et al., "Ectopic Expression of <i>Hoxb-8</i> Causes Duplication of the ZPA in the Forelimb and Homeotic Transformation of Axial Structures", <i>Cell</i> <u>78</u> :589-601 (1994).		
BA	Coffman et al., "Xotch, the Xenopus homolog of Drosophila notch", <i>Science</i> <u>249</u> :1438-1441 (1990)		
BB	Concordet, J. and Ingham, P., "Developmental biology. Patterning goes sonic", <i>Nature</i> <u>375</u> (6529):279-280 (May 1995)		
BC	Currie et al., "Induction of a specific muscle cell type by a hedgehog-like protein in zebrafish", <i>Nature</i> <u>383</u> :452-455 (1996)		
BD	Curry et al., "Sequence analysis reveals homology between two proteins of the flagellar radial spoke", <i>Mol. Cell. Biol.</i> <u>12</u> :3967-3977 (1992)		
BE	Davidson, E.H., "How embryos work: a comparative view of diverse modes of cell fate specification", <i>Devel.</i> <u>108</u> :365-389 (1990)		
BF	Davis, A.P. and M.R. Capecchi, "Axial homeosis and appendicular skeleton defects in mice with a targeted disruption of <i>hoxd-1</i> ", <i>Devel.</i> <u>120</u> :2187-2198 (1994)		
BG	Dickinson W., "Molecules and morphology: Where's the homology", <i>TIG</i> <u>11</u> , (4):119-120 (1995)		
BH	Dingemans, M.A. et al., "The expression of liver-specific genes within rat embryonic hepatocytes is a discontinuous process", <i>Differentiation</i> <u>56</u> :153-162 (1994)		
BI	Dollé, P. et al., "Coordinate expression of the murine <i>Hox-5</i> complex homoeobox-containing genes during limb pattern formation", <i>Nature</i> <u>342</u> :767-772 (1989)		
BJ	Dollé, P. et al., "Disruption of the <i>Hoxd-13</i> gene induces localized heterochrony leading to mice with neotenic limbs", <i>Cell</i> <u>75</u> :431-441 (1993)		
BK	Echelard, Y. et al., "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity", <i>Cell</i> <u>75</u> :1417-1430 (1993)		
BL	Ekker, S. et al., "Distinct expression and shared activities of members of the hedgehog gene family of xenopus laevis", <i>Devel.</i> <u>121</u> (8):2337-2347 (Aug 1995)		
BM	Ericson, J. et al., "Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube", <i>Cell</i> <u>81</u> (5):747-756 (June 1995)		
BN	Ettelaie, C. et al., "The effect of lipid peroxidation and lipolysis on the ability of lipoproteins to influence thromboplastin activity", <i>Biochim. Biophys. Acta.</i> <u>1257</u> (1):25-30 (June 1995)		
BO	Fahrner, K. et al., "Transcription of <i>H-2</i> and <i>Qa</i> genes in embryonic and adult mice", <i>EMBO J.</i> <u>6</u> :1265-1271 (1987)		
BP	Fallon, J.F. et al., "FGF-2: Apical ectodermal ridge growth signal for chick limb development", <i>Science</i> <u>264</u> :104-107 (1994)		
BQ	Fan, C. et al., "Long-range sclerotome induction by sonic hedgehog: Direct role of the amino-terminal cleavage product and modulation by the cyclic AMP signaling pathway", <i>Cell</i> <u>81</u> :457-465 (5 May 1995)		
BR	Fietz, M. et al., "The hedgehog gene family in Drosophila and vertebrate development", <i>Devel. Supp.</i> 43-51 (1994)		
BS	Forbes, A.J. et al., "Genetic analysis of <i>hedgehog</i> signalling in the <i>Drosophila</i> embryo", <i>Devel.</i> <u>119</u> (Supp.):115-124 (1993)		
EXAMINER		DATE CONSIDERED	
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.			

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Form PTO-1449		Docket Number (Optional) HMV-006.12	Application Number 08/954,128
INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Applicant Ingham, Philip, et al.	
		Filing Date 20 October 1997	Group Art Unit
OTHER DOCUMENTS <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>			
BT	Francis, P.H. et al., "Bone morphogenetic proteins and a signalling pathway that controls patterning in the developing chick limb", <i>Devel.</i> <u>120</u> :209-218 (1994)		
BU	Gallop, M. et al., "Applications of combinatorial technologies to drug discovery. 1. Background and peptide combinatorial libraries", <i>J. of Med. Chem.</i> <u>37</u> (9):1233-1251 (1994)		
BV	Gérard, M. et al., "Structure and activity of regulatory elements involved in the activation the the <i>Hoxd-11</i> gene during late gastrulation", <i>EMBO J.</i> <u>12</u> :3539-3550 (1993)		
BW	Gurdon, J.B., "The Generation of diversity and pattern in animal development", <i>Cell</i> <u>68</u> :185-199 (1992)		
BX	Gustin, K. et al., "Characterization of the role of individual protein binding motifs within the hepatitis B virus enhancer 1 on X promoter activity using linker scanning mutagenesis", <i>Virology</i> <u>193</u> :653-660 (1993)		
BY	Hall, T., et al., "A potential catalytic site revealed by the 1.7-A crystal structure of the amino-terminal signalling domain of Sonic hedgehog", <i>Nature</i> <u>378</u> (6553):212-216 (Nov 1995)		
BZ	Halpern, M.E., et al., "Induction of muscle pioneers and floor plate is distinguished by the zebrafish <i>no tail</i> mutation", <i>Cell</i> <u>75</u> :99-111 (1993)		
CA	Hamburger, V. and H.L. Hamilton, "A series of normal stages in the development of the chick embryo", <i>J. Morph.</i> <u>88</u> :49-92 (1951)		
CB	Hammerschmidt, M. et al., "The world according to hedgehog", <i>TIG</i> <u>13</u> (1):14-21 (1997)		
CC	Haramis, A. et al., "The limb deformity mutation disrupts the SHH/FGF-4 feedback loop and regulation of 5-HoxD genes during limb pattern formation", <i>Devel.</i> <u>121</u> (12):4161-4170 (Dec 1995)		
CD	Hardy, A., et al., "Gene expression, polarising activity and skeletal patterning in reaggregated hind limb mesenchyme", <i>Devel.</i> <u>121</u> (12):4329-4337 (Dec 1995)		
CE	Hatta, K. et al., "The cyclops mutation blocks specification of the floor plate of the zebrafish central nervous system", <i>Nature</i> <u>350</u> :339-341 (1991)		
CF	Heberlein, U. et al., "The TGB β homolog <i>dpp</i> and the segment polarity gene <i>hedgehog</i> are required for propagation of a morphogenetic wave in the <i>Drosophila</i> retina", <i>Cell</i> <u>75</u> :913-926 (1993)		
CG	Heemskerk, J. and S. DiNardo, " <i>Drosophila hedgehog</i> acts as a morphogen in cellular patterning", <i>Cell</i> <u>76</u> :449-460 (1994)		
CH	Hidalgo, A. and P. Ingham, "Cell patterning in <i>Drosophila</i> segment: spatial regulation of the segment polarity gene <i>patched</i> ", <i>Devel.</i> <u>110</u> :291-301 (1990)		
CI	Hooper, J. and Scott, M., "The <i>Drosophila</i> <i>patched</i> gene encodes a putative membrane protein required for segmental patterning", <i>Cell</i> <u>59</u> :751-765 (1989)		
CJ	Hynes, R.O., "Integrins: A family of Cell Surface Receptors", <i>Cell</i> <u>48</u> :549-554 (1987)		
CK	Hynes, M., et al., "Induction of midbrain dopaminergic neurons by Sonic hedgehog", <i>Neuron</i> <u>15</u> (1):35-44 (July 1995)		
CL	Ingham, P.W., "Signalling by hedgehog family proteins in <i>Drosophila</i> and vertebrate developmenr", <i>Curr. Opin. Genet. Dev.</i> <u>5</u> (4):478-484 (Aug 1995)		
CM	Ingham, P.W., " <i>Hedgehog</i> points the way", <i>Current Biology</i> <u>4</u> (4):347-350 (1994)		
CN	Ingham, P.W., "Localized <i>hedgehog</i> activity controls spatial limits of <i>wingless</i> transcription in the <i>Drosophila</i> embryo", <i>Nature</i> <u>366</u> :560-562 (1993)		
EXAMINER		DATE CONSIDERED	
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP \square 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.			

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

LIB_3 /0120934.01

Form PTO-1449

**INFORMATION DISCLOSURE CITATION
IN AN APPLICATION**
(Use several sheets if necessary)

Docket Number (Optional)

HMV-006.12

Application Number

08/954,128

Applicant **Ingham, Philip, et al.**

Filing Date

20 October 1997

Group Art Unit

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

CO	Ingham, P.W. and A. Hidalgo, "Regulation of <i>wingless</i> transcription in the <i>Drosophila</i> embryo", <i>Devel.</i> 117 :283-291 (1993)
CP	Ingham, P.W. et al., "Role of the <i>Drosophila</i> <i>patched</i> gene in positional signalling", <i>Nature</i> 353 :184-187 (1991)
CQ	Izpisua-Belmonte, J.-C. et al., "Expression of the homeobox <i>Hox-4</i> genes and the specification of position in chick wing development", <i>Nature</i> 350 :585-589 (1991)
CR	Izpisua-Belmonte, J.-C. et al., "Expression of <i>Hox-4</i> genes in the chick wings links pattern formation to the epithelial-mesenchymal interactions that mediate growth", <i>EMBO J.</i> 11 :1451-1457 (1992)
CS	Jiang, J. and Struhl, G., "Protein kinase A in hedgehog signalling in <i>Drosophila</i> limb development", <i>Cell</i> 80 (4):563-572 (Feb 1995)
CT	Jessel, T.M. and D.A. Melton, "Diffusible factors in vertebrate embryonic induction", <i>Cell</i> 68 :257-270 (1992)
CU	Johnson, R.L. and C. Tabin, "The long and short of <i>hedgehog</i> signaling", <i>Cell</i> 81 :313-315 (5 May 1995)
CV	Johnson, R.L. et al., "Patched overexpression alters wing disc size and pattern: transcriptional and post-transcriptional effects on <i>hedgehog</i> targets", <i>Devel.</i> 121 (12):4237-4245 (Dec 1995)
CW	Johnson, R.L., et al., "Ectopic expression of Sonic hedgehog alters dorsal-ventral patterning of somites", <i>Cell</i> 79 (7):1165-1173 (Dec 1994)
CX	Johnson, R.L. et al., "Mechanism of limb patterning", <i>Curr. Opin. Genet. Dev.</i> 4 (4):535-542 (Aug 1994)
CY	Johnson, R.L. et al., "Sonic hedgehog: a key mediator of anterior-posterior patterning of the limb and dorso-ventral patterning of axial embryonic structures", <i>Biochem. Soc. Trans.</i> 22 (3):569-574 (Aug 1994)
CZ	Jones, M. et al., "Involvement of bone morphogenetic protein-4 (BMP-4) and Vgr-L in morphogenesis and neurogenesis in the mouse", <i>Devel.</i> 111 :531-542 (1991)
DA	Kalderon, D., "Morphogenetic signaling. Responses to <i>hedgehog</i> ", <i>Curr. Biol.</i> 5 (6):580-582 (June 1995)
DB	Koonin, E., "A protein splice-junction motif in <i>hedgehog</i> family proteins", <i>Trends in Biochem. Sci.</i> 20 (4):141-142 (April 1995)
DC	Kornblihtt, A.R. et al., "Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene", <i>EMBO J.</i> 4 :1755-1759 (1985)
DD	Kornfeld, R. and S. Kornfeld, "Assembly of asparagine-Linked oligosaccharides", <i>Ann. Rev. Biochem.</i> 54 :631-664 (1985)
DE	Krauss, S. et al., "Expression of the zebrafish paired box gene <i>pax[xf-b]</i> during early neurogenesis", <i>Devel.</i> 113 :1193-1206 (1991)
DF	Krauss, S. et al., "A functionally conserved homolog of the <i>Drosophila</i> segment polarity gene <i>hh</i> is expressed in tissues with polarizing activity in zebrafish embryos", <i>Cell</i> 75 :1431-1444 (1993)
DG	Lai, C. et al., "Patterning of the neural ectoderm of <i>Xenopus laevis</i> by the amino-terminal product of <i>hedgehog</i> autoproteolytic cleavage", <i>Devel.</i> 121 (8):2349-2360 (Aug 1995)
DH	Laufer, E. et al., " <i>Sonic hedgehog</i> and <i>Fgf-4</i> act through a signaling cascade and feedback loop to integrate growth and patterning of the developing limb bud", <i>Cell</i> 79 :993-1003 (16 Dec. 1994)
DI	Lee, J.J. et al., "Secretion and localized transcription suggest a role in positional signaling for products of the segmentation gene <i>hedgehog</i> ", <i>Cell</i> 71 :33-50 (1992)
DJ	Lee, J. et al., "Autoproteolysis in <i>hedgehog</i> protein biogenesis", <i>Science</i> 266 (5190):1528-1537 (Dec 1994)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Docket Number (Optional) HMV-006.12	Application Number 08/954,128
		Applicant Ingham, Philip, et al.	
		Filing Date 20 October 1997	Group Art Unit
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
DK	Levin, M. et al., "A molecular pathway determining left-right asymmetry in chick embryogenesis", <i>Cell</i> 82 (5):803-814 (Sept 1995)		
DL	Li, W. et al., "Function of protein kinase A in hedgehog signal transduction and Drosophila imaginal disc development", <i>Cell</i> 80 (4):553-562 (Feb 1995)		
DM	Lopez-Martinez, A. et al., "Limb-patterning activity and restricted posterior localization of the amino-terminal product of Sonic hedgehog cleavage", <i>Curr. Biol.</i> 5 (7):791-796 (July 1995)		
DN	Lumsden, A. and Graham, A., "Neural patterning: A forward role for hedgehog", <i>Curr. Biol.</i> 5 (12):1347-1350 (Dec 1995)		
DO	Ma, C. et al., "The segment polarity gene <i>hedgehog</i> is required for progression of the morphogenetic furrow in the developing Drosophila eye", <i>Cell</i> 75 :927-938 (1993)		
DP	Ma, C. and Moses, K., "Wingless and patched are negative regulators of the morphogenetic furrow and can affect tissue polarity in the developing Drosophila compound eye", <i>Devel.</i> 121 (8) 2279-2289 (Aug 1995)		
DQ	Marigo, V. et al., "Biochemical evidence that patched is the hedgehog receptor", <i>Nature</i> 384 : 176-179 (1996)		
DR	Maccabe, J.A. and B.W. Parker, "The target tissue of limb-bud polarizing activity in the induction of supernumerary structures", <i>J. Embryol. Exp. Morph.</i> 53 :67-73 (1979)		
DS	Marti, E. et al., "Distribution of Sonic hedgehog peptides in the developing chick and mouse embryo", <i>Devel.</i> 121 (8):2537-2547 (Aug 1995)		
DT	Marti, E. et al., "Requirement of 19K form of Sonic hedgehog for induction of distinct ventral cell types in CNS explants" <i>Nature</i> 375 (6529):322-325 (May 1995)		
DU	Mavillo, F. et al., "Activation of four homeobox gene clusters in human embryonal carcinoma cells induced to differentiate by retinoic acid", <i>Differentiation</i> 37 :73-79 (1988)		
DV	McGinnis, W. and R. Krumlauf, "Homeobox genes and axial patterning", <i>Cell</i> 68 :283-302 (1992)		
DW	Mohler, J., "Requirements for <i>hedgehog</i> , a segmental polarity gene, in patterning larval and adult cuticle of Drosophila", <i>Genetics</i> 120 :1061-1072 (1988)		
DX	Mohler, J. and K. Vani, "Molecular organization and embryonic expression of the <i>hedgehog</i> gene involved in cell-cell communication in segmental patterning of Drosophila", <i>Devel.</i> 115 :957-971 (1992)		
DY	Morgan, B.A. et al., "Targeted misexpression of <i>Hox-4.6</i> in the avian limb bud causes apparent homeotic transformations", <i>Nature</i> 358 :236-239 (1992)		
DZ	Munsterberg A. et al., "Combinatorial signaling by Sonic hedgehog and Wnt family members induces myogenic bHLH gene expression in the somite", <i>Genes Dev.</i> 9 (23):2911-2922 (Dec 1995)		
EA	Nakano, Y. et al., "A protein with several possible membrane-spanning domains encoded by the Drosophila segment polarity gene <i>patched</i> ", <i>Nature</i> 341 :508-513 (1989)		
EB	Ngo, J. et al., "The protein folding problem and tertiary structure prediction", Merz and LeGrand, ed. Birkhauser, Boston (1994)		
EC	Niswander, L. and G.R. Martin, "FGF-4 and BMP-2 have opposite effects on limb growth", <i>Nature</i> 361 :68-71 (1993)		
ED	Niswander, L. et al., "A positive feedback loop coordinates growth and patterning in the vertebrate limb", <i>Nature</i> 371 (6498): 609-612 (Oct 1994)		
EE	Nohno, T. et al., "Involvement of the <i>Chox-4</i> chicken homeobox genes in determination of anteroposterior axial polarity during limb development", <i>Cell</i> 64 :1197-1205 (1991)		
EF	Nohno, T. et al., "Involvement of the Sonic hedgehog gene in chick feather formation", <i>Biochem. Biophys. Res. Comm.</i> 206 (1): 33-39 (Jan 1995)		
EG	O'Farrell, P.H., "Unanimity waits in the wings", <i>Nature</i> 368 :188-189 (1994)		
EXAMINER		DATE CONSIDERED	
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.			

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Form PTO-1449		Docket Number (Optional) HMV-006.12	Application Number 08/954,128
INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Applicant Ingham, Philip, et al.	
		Filing Date 20 October 1997	Group Art Unit
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
EH	Parr, B.A. et al., "Mouse <i>Wnt</i> genes exhibit discrete domains of expression in the early embryonic CNS and limb buds", <i>Devel.</i> <u>119</u> :247-261 (1993)		
EI	Patel, N.H. et al., "The role of segment polarity genes during <i>Drosophila</i> neurogenesis", <i>Genes Devel.</i> <u>3</u> :890-904 (1989)		
EJ	Peifer, M., "The two faces of hedgehog", <i>Science</i> <u>266</u> (5190):1492-1493 (Dec 1994)		
EK	Perrimon, N., "Hedgehog and beyond", <i>Cell</i> <u>80</u> :517-520 (24 Feb.1995)		
EL	Pham, A. et al., "The suppressor of fused gene encodes a novel PEST protein involved in <i>Drosophila</i> segment polarity establishment", <i>Genetics</i> <u>140</u> (2):587-598 (June 1995)		
EM	Placzek, M. et al., "Induction of floor plate differentiation by contact-dependent, homeogenetic signals", <i>Devel.</i> <u>117</u> :205-218 (1993)		
EN	Placzek, M. et al., "Orientation of commissural axons <i>in vitro</i> in response to a floor plate-derived chemoattractant", <i>Devel.</i> <u>110</u> :19-30 (1990)		
EO	Pollack, R.A. et al., "Altering the boundaries of <i>Hox3.1</i> expression: Evidence for antipodal gene regulation", <i>Cell</i> <u>71</u> :911-923 (1992)		
EP	Porter, J. et al., "The product of hedgehog autoproteolytic cleavage active in local and long-range signalling", <i>Nature</i> <u>374</u> (6520):363-366 (Mar 1995)		
EQ	Reeck et al., "Homology in proteins and nucleic acids: A terminology muddle and a way out of it", <i>Cell</i> <u>50</u> :667 (1987)		
ER	Rennie, J., "Super Sonic", <i>Scientific American</i> :20 (April 1994)		
ES	Riddle, R.D. et al., " <i>Sonic hedgehog</i> Mediates the Polarizing Activity of the ZPA", <i>Cell</i> <u>75</u> :1401-1416 (1993)		
ET	Riddle, R.D. et al., "Induction of the LIM homeobox gene <i>Lmx1</i> by WNT7a establishes dorsoventral pattern in the vertebrate limb", <i>Cell</i> <u>83</u> (6553):212-216 (Nov 1995)		
EU	Riley, B.B. et al., "Retroviral expression of FGF-2 (bFGF) affects patterning in chick limb bud", <i>Devel.</i> <u>118</u> :95-104 (1993)		
EV	Roberts, D. et al., "Sonic hedgehog is an endothermal signal inducing Bmp-4 and Hox genes during induction and regionalization of the chick hindgut", <i>Devel.</i> <u>121</u> (10): 3163-74 (Oct 1995)		
EW	Roelink, H. et al., "Floor plate and motor neuron Induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog autoproteolysis", <i>Cell</i> <u>81</u> :445-455 (5 May 1995)		
EX	Roelink, H. et al., Floor plate and motor neuron induction by vhh-1, a Vertebrate Homolog of <i>hedgehog</i> expressed by the notochord", <i>Cell</i> <u>76</u> :761-775 (1994)		
EY	Sambrook et al., <i>Molecular Cloning CSH</i> :11.47 (1989)		
EZ	Sasaki, H. and B.L.M. Hogan, "Differential expression of multiple fork head related genes during gastrulation and axial pattern formation in the mouse embryo", <i>Devel.</i> <u>118</u> :47-59 (1993)		
FA	Savage, M. et al., "Distribution of FGH-2 suggests it has a role in chick limb bud growth", <i>Devel. Dynamics</i> <u>198</u> :159-170 (1993)		
FB	Schuske, K. et al., " <i>Patched</i> overexpression causes loss of <i>wingless</i> expression in drosophila embryos", <i>Devel. Biol.</i> <u>164</u> :300-311 (1994)		
EXAMINER		DATE CONSIDERED	
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP α 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.			

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Form PTO-1449

**INFORMATION DISCLOSURE
CITATION
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number (Optional)

HMV-006.12

Application Number

08/954,128

Applicant: Ingham, Philip, et al.

Filing Date: 20 October 1997

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

FC	Smith, J.C., "Hedgehog, the floor plate, and the zone of polarizing activity", <i>Cell</i> <u>76</u> :193-196 (1994)
FD	Stachel, S.E. et al., "Lithium perturbation and <i>goosecoid</i> expression identify a dorsal specification pathway in the pregastrula zebrafish", <i>Devel.</i> <u>117</u> :1261-1274 (1993)
FE	Stolow, M. and Shi, Y., <i>Xenopus</i> sonic hedgehog as a potential morphogen during embryogenesis and thyroid hormone-dependent metamorphosis, <i>Nucleic Acids Res.</i> <u>23</u> (13):2555-1562 (July 1995)
FF	Stratagene 1988 cDNA libraries
FG	Tabata, T. and T.B. Kornberg, "Hedgehog Is a signaling protein with a key Role in patterning <i>Drosophila</i> imaginal discs", <i>Cell</i> <u>76</u> :89-102 (1994)
FH	Tabata, T. et al., "The <i>Drosophila hedgehog</i> gene is expressed specifically in posterior compartment cells and is a target of <i>engrailed</i> regulation", <i>Genes Devel.</i> <u>6</u> :2635-2645 (1992)
FI	Tabin, C.J., "Retinoids, homeoboxes, and growth factors: Toward molecular models for limb development", <i>Cell</i> <u>66</u> :199-217 (1991)
FJ	Tanebe, Y. et al., "Induction of motor neurons by Sonic hedgehog is independent of floor plate differentiation", <i>Curr. Biol.</i> <u>5</u> (6): 651-658 (June 1995)
FK	Tanaka, E. and Gann, A., "Limb development", <i>Curr. Biol.</i> <u>5</u> (6):594-597 (June 1995)
FL	Tashiro, S. et al., "Structure and expression of <i>hedgehog</i> , a <i>Drosophila</i> segment-polarity gene required for cell-cell communication", <i>Gene</i> <u>124</u> :183-189 (1993)
FM	Taylor, A.M. et al., "Contrasting distributions of patched and hedgehog proteins in the <i>Drosophila</i> embryo", <i>Mech. Dev.</i> <u>42</u> :89-96 (1993)
FN	Thaller, C. and G. Eichele, "Identification and spatial distribution of retinoids in the developing chick limb bud", <i>Nature</i> <u>327</u> :625-628 (1987)
FO	Tickle, C. et al., "A Quantitative Analysis of the Effect of all- <i>trans</i> -Retinoic Acid on the Pattern of Chick Wing Development", <i>Devel. Biol.</i> <u>109</u> :82-95 (1985)
FP	Tickle, C., "Vertebrate limb development", <i>Curr. Opin. Genet. Dev.</i> <u>5</u> (4):478-484 (Aug 1995)
FQ	Tickle, C. and Eichele, G., "Vertebrate limb development", <i>Ann. Rev. Cell Biol.</i> <u>10</u> :121-152 (1994)
FR	van Straaten, H.W.M. et al., "Effect of the notochord on the differentiation of a floor plate area in the neural tube of the chick embryo," <i>Anat. Embryol.</i> <u>177</u> :317-324 (1988)
FS	Vogel, A. and C. Tickle, "FGF-4 maintains polarizing activity of posterior limb bud cells in vivo and in vitro", <i>Devel.</i> <u>119</u> :199-206 (1993)
FT	Wallace et al., "Oligonucleotide probes for the screening of recombinant DNA libraries", <i>Methods in Enzymology</i> <u>152</u> :432 (1987)
FU	Wanek, N. et al., "Conversion by retinoic acid of anterior cells into ZPA cells in the chick wing bud", <i>Nature</i> <u>350</u> :81-83 (1991)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Docket Number (Optional)
HMV-006.12

Application Number
08/954,128

Applicant: Ingham, Philip, et al.

Filing Date: 20 October 1997

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

[illegible]

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.

Notice of References Cited	Application/Control No.	Applicant(s)/Patent Under Reexamination	
	08/954,128	Ingham, ET AL.	
	Examiner	Art Unit	Page 1 of 1
	Claire M. Kaufman	1646	

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	DOCUMENT SOURCE **	
							APS	OTHER
<input type="checkbox"/>	A	4,774,322	09/1988	Seydel et al.			<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	B						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	C						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	D						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	E						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	F						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	G						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	H						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	I						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	J						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	K						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	L						<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	M						<input type="checkbox"/>	<input type="checkbox"/>

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS	DOCUMENT SOURCE **	
								APS	OTHER
<input type="checkbox"/>	N							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	O							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	P							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Q							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	R							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	S							<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	T							<input type="checkbox"/>	<input type="checkbox"/>

NON-PATENT DOCUMENTS

*		DOCUMENT (Including Author, Title Date, Source, and Pertinent Pages)	DOCUMENT SOURCE **	
			APS	OTHER
<input type="checkbox"/>	U	Iwamoto et al., Actions of hedgehog proteins on skeletal cells, Crit. Rev. Oral Biol. Med., 10(4):477-486, 1999 (abstract).	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	V	Iwasaki et al., Age-dependent effects of hedgehog protein on chondrocytes, J. Bone Joint Surg. Br., 81(6):1076-1082, Nov. 1999 (abstract).	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	W	Katsuura et al., The NH2-terminal region of the active domain of sonic hedgehog is necessary for its signal transduction, FEBS Lett., 447(2-3):325-328, March 1999 (abstract).	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	X	Williams et al., Functiona antagonists of sonic hedgehog reveal the importance of the N terminus for activity, J. Cell Sci., 112(Pt 23):4405-4414, Dec. 1999 (abstract).	<input type="checkbox"/>	<input type="checkbox"/>

*A copy of this reference is not being furnished with this Office action. (See Manual of Patent Examining Procedure, Section 707.05(a).)

**APS encompasses any electronic search i.e. text, image, and Commercial Databases.

U.S. Patent and Trademark Office

PTO-892 (Rev. 03-98)

Notice of References Cited

Part of Paper No. 22

Form PTO-1449

INFORMATION DISCLOSURE CITATION**IN AN APPLICATION***(Use several sheets if necessary)*Docket Number (Optional)
HMSU-P12-006Application Number
08/954128Applicant
Ingham et al.Filing Date
20-Oct-1997Group Art Unit
1646**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation	
						YES	NO

OTHER DOCUMENTS*(Including Author, Title, Date, Pertinent Pages Etc.)*

	AA	Chang et al., "Products, genetic linkage, and limb patterning activity of a murine <i>hedgehog</i> gene", Development 120: 3339-3353 (1994).

EXAMINER

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.